

Amendments to the Specification

Please replace the paragraph beginning at page 16, line 16, with new paragraph as follows:

Turning now to the accompanying Figures, and in particular FIGS. 1-4, there ~~[[is]]~~are illustrated first and second embodiments of an implantable in vivo sensor in accordance with the present invention.

Please replace the paragraph beginning at page 16, line 20, with new paragraph as follows:

The inventive in vivo temperature sensor **10** consists generally of an implantable tubular member **12** having a central lumen **14**, an abluminal wall surface **16**, a luminal wall surface **18** and at least one of a plurality of sensor regions **20** integral with at least one of the abluminal wall surface **16** and the luminal wall surface **18** of the implantable tubular member **12**. The flow vector **F** of a fluid over the surface of the sensor region **20** is illustrated in FIG. 3. Each of the at least one of a plurality of sensor regions **20** further comprise a plurality of cantilever members **22** patterned in an array on the implantable tubular member **12**. The implantable tubular member **12**, the sensor **20** and the plurality of cantilever members **22** may be fabricated of like materials, such as shape memory materials, or may be fabricated of different materials, e.g., the implantable tubular member **12** being fabricated of stainless steel and the sensor **20** and cantilever members **22** being fabricated of a shape memory material, such as nickel-titanium alloys. In accordance with the best mode contemplated for the present invention, the tubular member **12**, the sensor **20** and the cantilever members **22** will be fabricated of shape memory materials, such as nickel-titanium alloys. Where each of the plurality of cantilever members **22** are fabricated of a shape memory material, either individual cantilever members **22** or groups of cantilever members **22** within a single sensor **20** may be fabricated to have different martensite transition temperatures. Thus, for example, cantilever members **22a** within sensor **20** may be fabricated to have a transition temperature of X degrees Centigrade, while cantilever members **22b** are fabricated to have a transition temperature of $X+1$ degrees Centigrade, cantilever members **22c** are fabricated to have a transition temperature of $X+2$ degrees Centigrade, etc. Alternatively all of the cantilever members **22** in a sensor **20** may have the same transition

temperature, and a plurality of sensors **20** are provided such that sensor **20a** has cantilever members 22 having a transition temperature of X degrees Centigrade, while the plurality of cantilever members **22** in sensor **20b** are fabricated to have a transition temperature of X+1 degrees Centigrade, and the plurality of cantilever members **22** in sensor **20c** are fabricated to have a transition temperature of X+2 degrees Centigrade, etc.

Please replace the paragraph beginning at page 17, line 18, with new paragraph as follows:

Each of the plurality of cantilever members **22** may be fabricated of a material capable of undergoing elastic, plastic, shape memory and/or a superelastic deformation. Materials such as stainless steel, titanium, nickel, tantalum, gold, vanadium, nickel-titanium, or alloys thereof may be employed to fabricate the plurality of cantilever members 22. Different electrical, thermal or mechanical properties may be imparted to the cantilever members **22** by altering the alloy ratios of the material. It is preferable to vacuum deposit both the tubular member **12**, the sensors **20** and the cantilever members **22** to permit tight control over the material composition, electrical, mechanical and thermal properties of the material, as well as provide for tight control over the tissue and fluid contacting surfaces and the bulk material of the device. For example with nickel-titanium alloys, the titanium content of the target, in a nickel-titanium binary target, may be changed a known amount to precisely alter the transition temperature of a cantilever members 22.

Please replace the paragraph beginning at page 18, line 1, with new paragraph as follows:

Each of the plurality of cantilever members **22** preferably have binary functionality to provide a first “off” position indicative of an austenite phase of the cantilever members **22** and a second “on” position indicative of a martensite phase of the cantilever members **22**. The first “off” position may be configured such that it is in a raised position which projects outwardly relative to the sensor **20** and/or the tubular member 12 or in the lowered position that is substantially co-planar with the sensor **20** and/or the tubular member **12**. Similarly, the second “on” position may be configured such that it is in a lowered position that is substantially coplanar with the sensor **20** and/or the tubular member **12** or the cantilever members **22** may be in the raised position or projecting outwardly relative to the sensor **20** and the tubular member **12**,

provided, however, that the first “on” position and the second “off” positions are different from one and other.

Please replace the paragraph beginning at page 18, line 12, with new paragraph as follows:

It will be understood, therefore, that as the implanted temperature sensor 10 encounters different in vivo temperatures, different sets of cantilever members 22 will be exposed to their transition temperature and change from the “off” position to the “on” position. In order to detect which cantilever members 22 are in the “on” position and, therefore, determine the in vivo thermal conditions, the temperature sensor 10 may be imaged radiographically, ultrasonically, magnetically or may be exposed to an external energy source which returns a signal representative of the number and position of the cantilever members 22 that are in the “on” position. The returned signal may be generated by a passive transmitter embedded in solid state circuitry defined within the sensor 20, wherein the cantilever members [[20]]22 serve as electromechanical switches which alter a property of the solid state circuitry, for example, impedance or capacitance, and which then returns a detectable signal representative of the number and position of cantilever members 22 in the “on” position.

Please replace the paragraph beginning at page 18, line 25, with new paragraph as follows:

Because it is structurally virtually identical to the temperature sensor 10, described above, the inventive in vivo pressure sensor will also be described with reference to FIGS. 1-4 and use identical reference numerals to describe the elements thereof. The inventive in vivo pressure sensor 10 consists generally of an implantable tubular member 12 having a central lumen 14, an abluminal wall surface 16, a luminal wall surface 18 and at least one of a plurality of sensor regions 20 integral with at least one of the abluminal wall surface 16 and the luminal wall surface 18 of the implantable tubular member 12. Each of the at least one of a plurality of sensor regions further comprise a plurality of cantilever members 22 patterned in an array on the implantable tubular member 12. The implantable tubular member 12, the sensor regions 20 and the plurality of cantilever members 22 may be fabricated of like materials, such as superelastic materials, or may be fabricated of different materials, e.g., the implantable tubular member 12

being fabricated of stainless steel and the sensor regions **20** and cantilever members **22** being fabricated of a superelastic material, such as nickel-titanium alloys. In accordance with the best mode contemplated for the present invention, the tubular member **12**, the sensor regions **20** and the cantilever members **22** will be fabricated of superelastic materials, such as nickel-titanium alloys. Where each of the plurality of cantilever members **22** are fabricated of a superelastic material, either individual cantilever members **22** or groups of cantilever members **22** within a single sensor regions **20** may be fabricated to have different martensite transition temperatures. Thus, for example, cantilever members **22a** within sensor **20** may be fabricated to have a martensitic stress/strain transition coefficient σ , while cantilever members **22b** are fabricated to have a transition coefficient $\sigma+1$, cantilever members **22c** are fabricated to have a transition coefficient of $\sigma+2$, etc. such that different cantilever members **22** or groups of cantilever members **22** change their position based upon a given quantum of stress or strain applied to the cantilever members **22** in vivo. Alternatively all of the cantilever members **22** in a sensor **20** may have the same transition temperature, and a plurality of sensors **20** are provided such that sensor **20a** has cantilever members **22** having a transition coefficient σ , while the plurality of cantilever members **22** in sensor **20b** are fabricated to have a transition coefficient of $\sigma+1$, and the plurality of cantilever members **22** in sensor **20c** are fabricated to have a transition coefficient of $\sigma+2$, etc. such that different sensors **20a**, **20b**, **20c** respond to different stress-strain conditions.

Please replace the paragraph beginning at page 19, line 25, with new paragraph as follows:

Each of the plurality of cantilever members **22** may be fabricated of a shape memory and/or a superelastic material. Different electrical, thermal or mechanical properties may be imparted to the cantilever members **22** by altering the alloy ratios of the material. It is preferable to vacuum deposit both the tubular member **12**, the sensors regions **20** and the cantilever members **22** to permit tight control over the material composition, electrical, mechanical and thermal properties of the material, as well as provide for tight control over the tissue and fluid contacting surfaces and the bulk material of the device. For example with nickel-titanium alloys, the titanium content of the target, in a nickel-titanium binary target, may be changed a known amount to precisely alter the transition temperature of a cantilever members **22**.

Please replace the paragraph beginning at page 20, line 4, with new paragraph as follows:

Each of the plurality of cantilever members **22** may have binary functionality to provide a first “off” position indicative of an austenite phase of the cantilever members **22** and a second “on” position indicative of a martensite phase of the cantilever members **22**. The first “off” position may be configured such that it is in a raised position which projects outwardly relative to the sensor regions 20 and/or the tubular member 12 or in the lowered position that is substantially co-planar with the sensor regions 20 and/or the tubular member **12**. Similarly, the second “on” position may be configured such that it is in a lowered position that is substantially coplanar with the sensor regions 0 and/or the tubular member **12** or the cantilever members **22** may be in the raised position or projecting outwardly relative to the sensor regions 20 and the tubular member **12**, provided, however, that the first “on” position and the second “off” positions are different from one and other.

Please replace the paragraph beginning at page 20, line 14, with new paragraph as follows:

Alternatively, rather than having merely binary functionality, each of the plurality of cantilever members **22** may have a response curve which is dependent upon the modulus of the material and the moment of inertia of each cantilever member 22. Each of the cantilever members **22** may be configured to have a variation in Z-axis thickness along an X-Y axis of the cantilever member **22**. By configuring the cantilever members **22** with variable Z-axis thicknesses, different cantilever members **22** or different groupings of cantilever members 22 will exhibit different stress-strain responses due to the different material modulus and different moment of inertia attendant to the altered geometry of the cantilever member **22**. With this alternate construct of the cantilever members **22**, for a given quantum of stress-strain applied to the cantilever members **22**, the cantilever members **22** will deflect and shift a returned resonance frequency applied from an external energy source. The degree of deflection will then correlate to the stress and strain forces acting upon the cantilever members **22**. It will be understood, of course, that this alternate construct of the cantilever members **22** still provides binary “on” and “off” functionality with the “on” and “off” positions merely being indicative of the outlying positions of the cantilever member **22**.

Please replace the paragraph beginning at page 21, line 1, with new paragraph as follows:

It will be understood, therefore, that as the implanted pressure sensor 10 encounters different stress and strain associated with, for example, changes in physiological blood pressure, fluid shear stress, endothelialization, arteriosclerotic plaque development, different sets of cantilever members 22 will be exposed to their transition conditions and change from the “off” position to the “on” position. In order to detect which cantilever members 22 are in the “on” position and, therefore, determine the stress-strain conditions, the pressure sensor 10 may be imaged radiographically, ultrasonically, magnetically or may be exposed to an external energy source which returns a signal representative of the number and position of the cantilever members 22 that are in the “on” position. The returned signal may be generated by a passive transmitter embedded in solid state circuitry defined within the sensor 20, wherein the cantilever members [[20]]22 serve as electromechanical switches which alter a property of the solid state circuitry, for example, impedance or capacitance, and which then returns a detectable signal representative of the number and position of cantilever members 22 in the “on” position.

Please replace the paragraph beginning at page 23, line 10, with new paragraph as follows:

Also with reference to FIGS. [[4]]5-7B there is illustrated a sensor device 30 which comprises a generally tubular member having a plurality of wall elements 32, 36 that define walls of the sensor device 30. The plurality of wall elements 32, 36 are preferably fabricated of shape memory or superelastic materials such that the endoluminal sensor device 30 effectively has at least two martensite transition points. Conventional shape memory and superelastic materials have a single martensite transition point. However, by fabricating all of the wall elements 32, 36 of laminates of shape memory or superelastic materials such that one ply has a martensite transition point of T_1 and a second ply has a martensite transition point of T_2 wherein $T_2 > T_1$, the first ply will cause the sensor device 30 to transition at T_1 which corresponds to the condition for normal in vivo physiological conditions, while the an additional quantum of energy, such as externally applied microwave, ultrasound, RF energy or internally applied energy, such as laser irradiation or direct thermal contact, will induce the condition suitable for transition at T_2 and the device will undergo a second shape transition. Alternatively, portions of the wall elements 32, 36 may be fabricated of a first material having a transition point T_1 , while

other portions of the wall elements **32, 36**, which are preferably non-structural for the sensor device **30** under the T_1 conditions, but are structural for the sensor device **30** under T_2 conditions, are fabricated of a second material having a transition point T_2 . Thus, those wall elements **32, 36** fabricate of the T_1 material will cause the sensor device **30** to transition into an initial endoluminal shape or geometry under the conditions appropriate to achieve transition point T_1 , while those wall elements **32, 36** fabricated of the T_2 material will not transition until the appropriate conditions for transition point T_2 are applied to the sensor device **30**.

Please replace the paragraph beginning at page 24, line 4, with new paragraph as follows:

Turning now to FIGS. 8-10 there is illustrated a biosensor **40** for sensing endothelialization events at the tissue-contacting surface of the sensor device. Like the inventive in vivo sensor devices described above, the inventive biosensor **40** consists generally of an implantable substrate carrier **42** having tissue contacting surfaces **42, 46, 48** thereupon. For purposes of illustration only, biosensor **40** is depicted with the implantable substrate carrier **42** being of a generally tubular configuration, such as for example, as stent. A plurality of binding regions **50** are defined on either of the tissue contacting surfaces **42, 46, 48**. The binding regions **50** are similar to the sensor regions of the above-described embodiments, except the binding regions **50** comprise regions of the implantable substrate carrier **42** which have biochemical markers, such as antibodies or ligands, bound thereto which are specific for endothelial and/or smooth muscle cell surface proteins or precursors of endothelial cell and smooth muscle cell proliferation, such as vascular endothelial growth factor or other growth factors. The material of the implantable substrate carrier **42** is preferably fabricated of a shape memory or superelastic material, which, upon binding of biological material to the biochemical markers in the binding regions **50**, undergoes phase transformation due either the binding to the biochemical markers alone or in combination with an applied energy to the bound complex. The phase transformation of the material of the implantable substrate carrier **42** will cause a frequency shift in a returned signal from the applied energy source and will be indicative of the bound state of the binding domains **50**.

Please replace the paragraph beginning at page 24, line 23, with new paragraph as follows:

With particular reference to co-pending, commonly assigned U.S. Patent Application Ser. No. 60/064,916, filed Nov. 7, 1997 which was published as PCT International Application WO9923977A1 entitled Intravascular Stent And Method For Manufacturing An Intravascular Stent, both of which are hereby incorporated by reference, the binding regions **50** may also form putative microgrooves [[50]]52 which are regions of the implantable substrate carrier **42** having patterned weakened atomic bonds in the crystalline structure of the substrate carrier **42** material. Upon binding of an endothelial cell, smooth muscle cell or a precursor thereof to the binding domain, the material of the substrate carrier **42** may either directly undergo or be induced by an external energy source to undergo a phase transformation which will cause the weakened atomic lattice of the crystalline structure of the substrate carrier **42** material to fracture and open a plurality of microgrooves **52** contiguous with the at the binding regions **50**. The microgrooves **52** may be propagated by the additional binding of biological material to the markers at the binding regions **50**. In this manner, there are self-propagating microgrooves 52 which facilitate endothelialization of the implanted substrate carrier 42.